AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning at page 2, line 10, with the following rewritten paragraph:

--Based upon this finding it is believed that p38, along with other MAPKs, have a role in mediating cellular response to inflammatory stimuli, such as leukocyte accumulation, macrophage/monocyte activation, tissue resorption, fever, acute phase responses and neutrophilia. In addition, MAPKs, such as p38, have been implicated in cancer, thrombin-induced platelet aggregation, immunodeficiency disorders, autoimmune diseases, cell death, allergies, osteoporosis and neurodegenerative disorders. Inhibitors of p38 have also been implicated in the area of pain management through inhibition of prostaglandin endoperoxide synthase-2 induction. Other diseases associated with [[Il-1]]IL-1, IL-6, IL-8 or TNF overproduction are set forth in WO 96/21654.--

Please replace the paragraph beginning at page 3, line 15, with the following rewritten paragraph:

--The rings that make up Q_1 are substituted with 1 to 4 substituents, each of which is independently selected from halo; C_1-C_3 alkyl optionally substituted with NR'_2, OR', CO_2R' or $CONR'_2$; O-(C_1-C_3)-alkyl optionally substituted with NR'_2, OR', CO_2R' or $CONR'_2$; NR'_2; OCF_3; CF_3; NO_2; CO_2R'; [[CONR']]CONHR'; SR'; $S(O_2)N(R')_2$; SCF_3; CN; $N(R')C(O)R^4$; $N(R')C(O)OR^4$; $N(R')C(O)C(O)R^4$; $N(R')S(O_2)R^4$; $N(R')R^4$; $N(R^4)_2$; OR^4; $OC(O)R^4$; $OP(O)_3H_2$; or [[N=C-$N(R')_2$]]N=CH-$N(R')_2$.--

Please replace the paragraph beginning at page 3, line 23, with the following rewritten paragraph:

--The rings that make up Q_2 are optionally substituted with up to 4 substituents, each of which is independently selected from halo; C_1-C_3 straight or branched alkyl optionally substituted with NR'_2, OR', CO_2R', $S(O_2)N(R')_2$, [[N=C-$N(R')_2$]]N=CH-$N(R')_2$, R^3, or $CONR'_2$; O-(C_1-C_3)-alkyl; O-(C_1-C_3)-alkyl optionally substituted with NR'_2, OR', CO_2R', $S(O_2)N(R')_2$, [[N=C-$N(R')_2$]]N=CH-$N(R')_2$, R^3, or $CONR'_2$; NR'_2; OCF_3; CF_3; NO_2; CO_2R'; [[CONR']]CONHR'; R^3; OR^3; [[NR^3]]NHR^3; SR^3; $C(O)R^3$; $C(O)N(R')R^3$; $C(O)OR^3$; SR'; $S(O_2)N(R')_2$; SCF_3; [[N=C-$N(R')_2$]]N=CH-$N(R')_2$; or CN.--

Please replace the paragraph beginning at page 5, line 1, with the following rewritten paragraph:

--R^2 is selected from hydrogen, (C_1-C_3)-alkyl, or [[(C_1-C_3)]](C_2-C_3)-alkenyl; each optionally substituted with -$N(R')_2$, -OR', SR', -C(O)-$N(R')_2$, -$S(O_2)$-$N(R')_2$, -C(O)-OR', or R^3.--

Please replace the paragraph beginning at page 6, line 8, with the following rewritten paragraph:

--The rings that make up Q_1 are substituted with 1 to 4 substituents, each of which is independently selected from halo; C_1-C_3 alkyl optionally substituted with NR'_2, OR', CO_2R' or $CONR'_2$; O-(C_1-C_3)-alkyl optionally substituted with NR'_2, OR', CO_2R' or $CONR'_2$;

NR'_2; OCF_3; CF_3; NO_2; CO_2R'; [[CONR']]CONHR'; SR'; $S(O_2)N(R')_2$; SCF_3; CN; $N(R')C(O)R^4$; $N(R')C(O)OR^4$; $N(R')C(O)C(O)R^4$; $N(R')S(O_2)R^4$; $N(R')R^4$; $N(R^4)_2$; OR^4; $OC(O)R^4$; $OP(O)_3H_2$; or [[N=C-$N(R')_2$]]N=CH-$N(R')_2$.--

Please replace the paragraph beginning at page 6, line 16, with the following rewritten paragraph:

--The rings that make up Q_2 are optionally substituted with up to 4 substituents, each of which is independently selected from halo; C_1-C_3 straight or branched alkyl optionally substituted with NR'_2, OR', CO_2R', $S(O_2)N(R')_2$, [[N=C-$N(R')_2$]]N=CH-$N(R')_2$, R^3, or $CONR'_2$; O-(C_1-C_3)-alkyl; O-(C_1-C_3)-alkyl optionally substituted with NR'_2, OR', CO_2R', $S(O_2)N(R')_2$, [[N=C-$N(R')_2$]]N=CH-$N(R')_2$, R^3, or $CONR'_2$; NR'_2; OCF_3; CF_3; NO_2; CO_2R'; [[CONR']]CONHR'; R^3; OR^3; [[NR^3]]NHR^3; SR^3; $C(O)R^3$; $C(O)N(R')R^3$; $C(O)OR^3$; SR'; $S(O_2)N(R')_2$; SCF_3; [[N=C-$N(R')_2$]]N=CH-$N(R')_2$; or CN.--

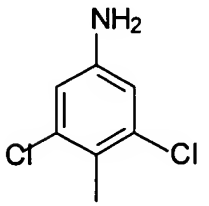
Please replace the paragraph beginning at page 8, line 3, with the following rewritten paragraph:

--R^2 is selected from hydrogen, (C_1-C_3)-alkyl, or [[(C_1-C_3)]](C_2-C_3)-alkenyl; each optionally substituted with -$N(R')_2$, -OR', SR', -C(O)-$N(R')_2$, -$S(O_2)$-$N(R')_2$, -C(O)-OR', or R^3.--

Please replace the paragraph beginning at page 8, line 9, with the following rewritten paragraph:

-- R_1 is selected from hydrogen, $(C_1$-$C_3)$-alkyl, OH, or O-$(C_1$-$C_3)$-alkyl. It will be apparent to those of skill in the art that if R_1 is OH, the resulting inhibitor may tautomerize resulting in[[a compound]] compounds of the formula:--

Please replace the chemical structures depicted at pages 10 and 11 with the following redrawn chemical structures:



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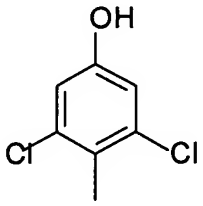

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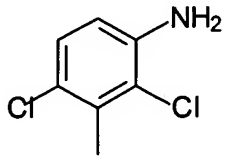

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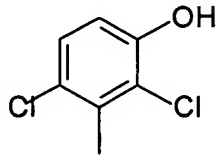

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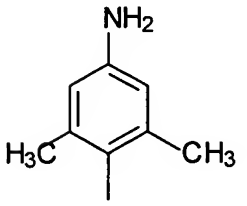

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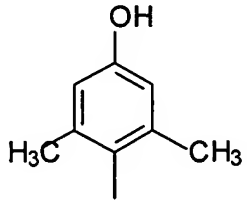

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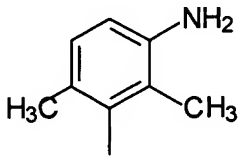

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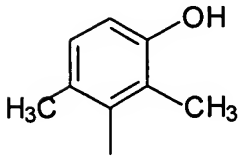

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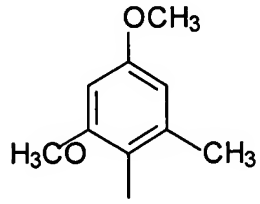

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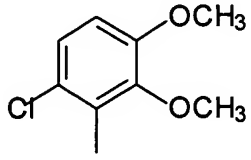

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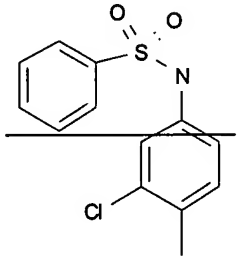
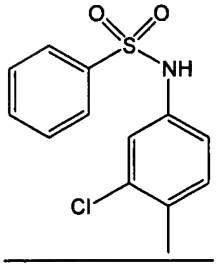
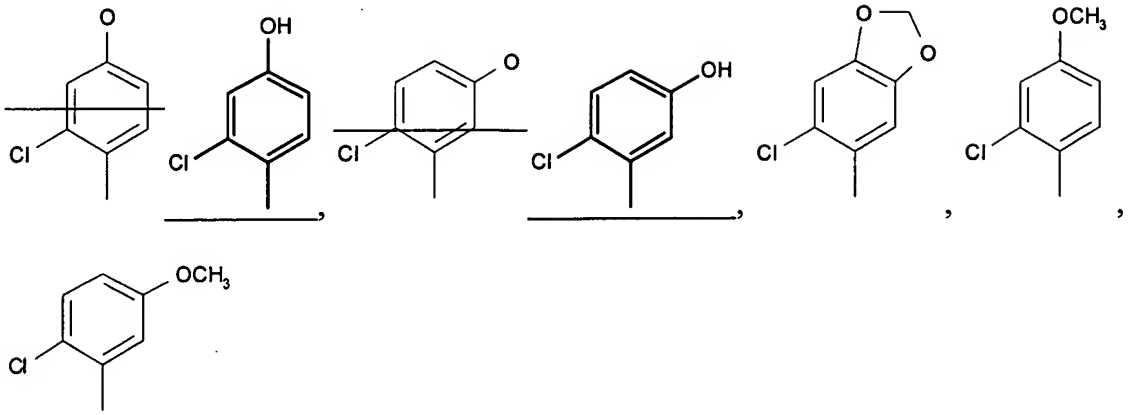
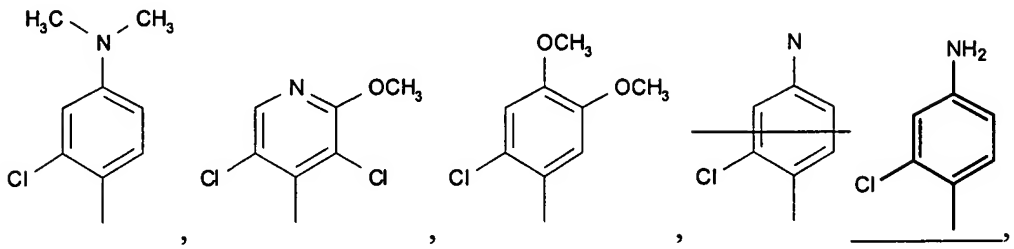
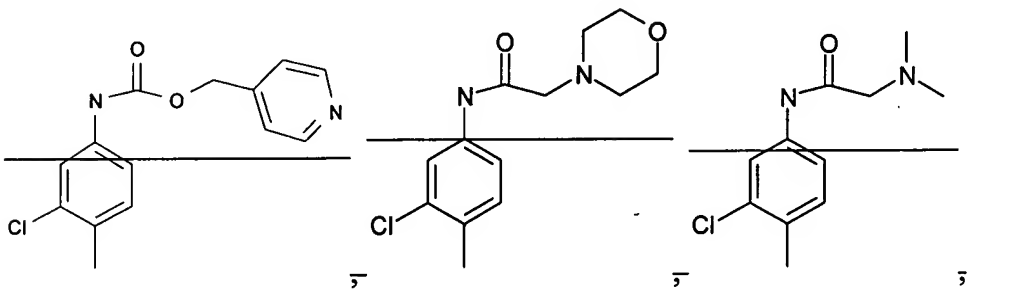
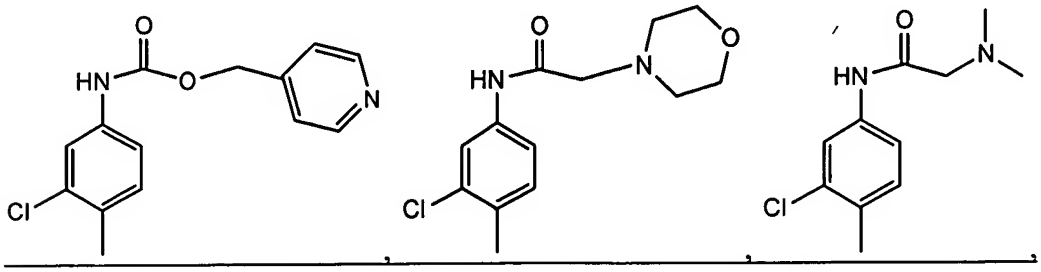


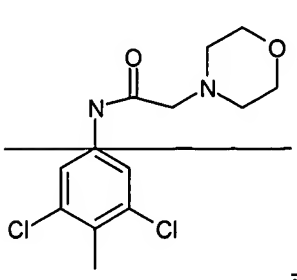
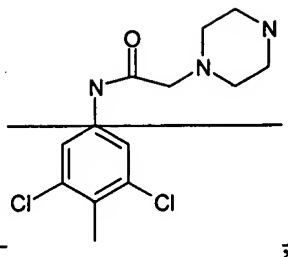
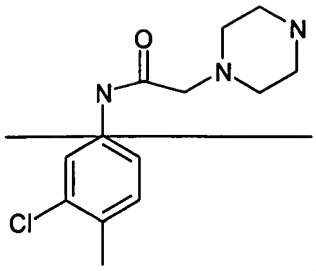


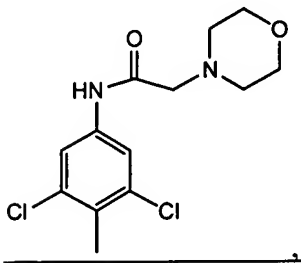
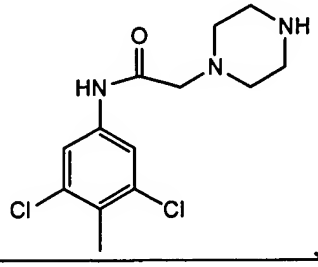
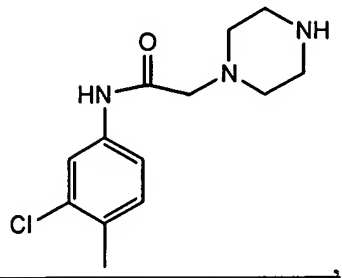


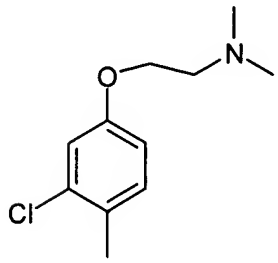
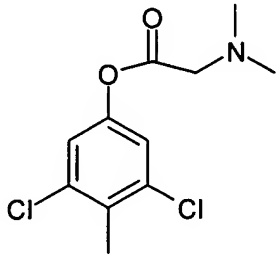
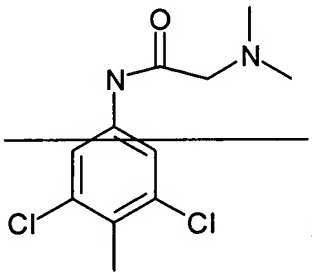
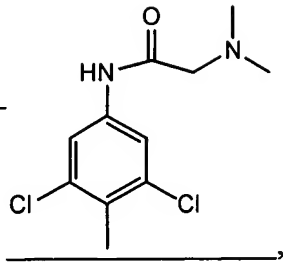


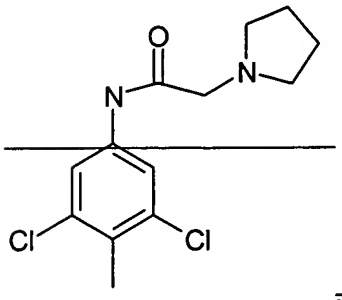
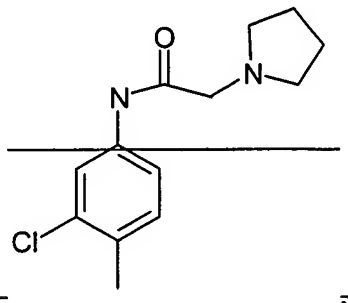
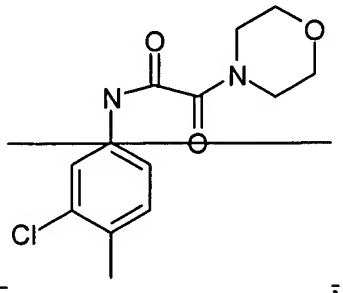


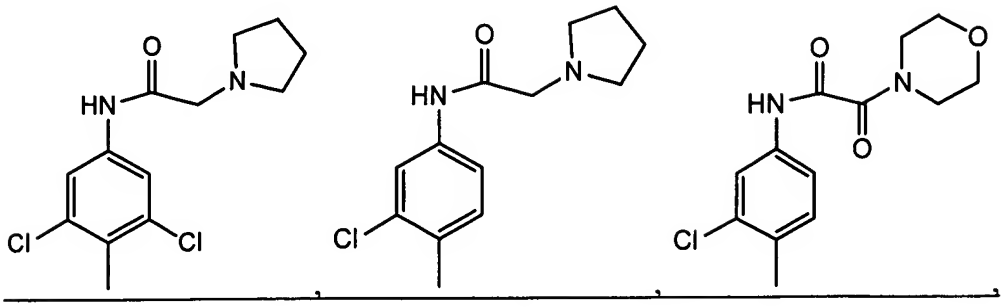
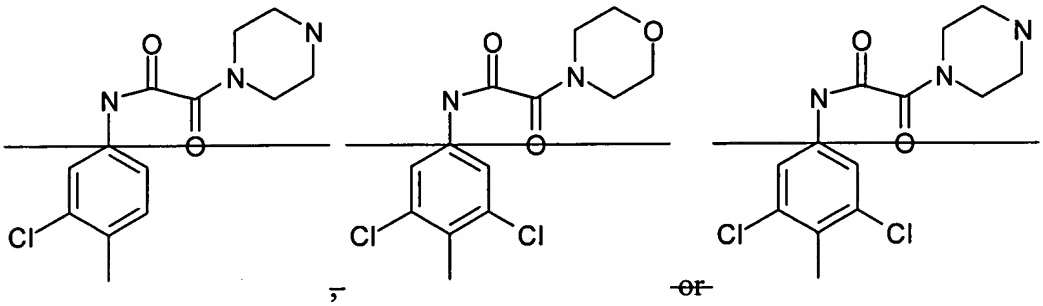
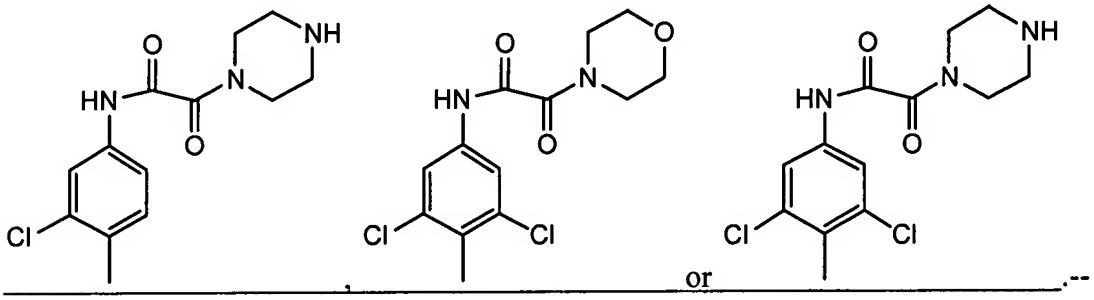


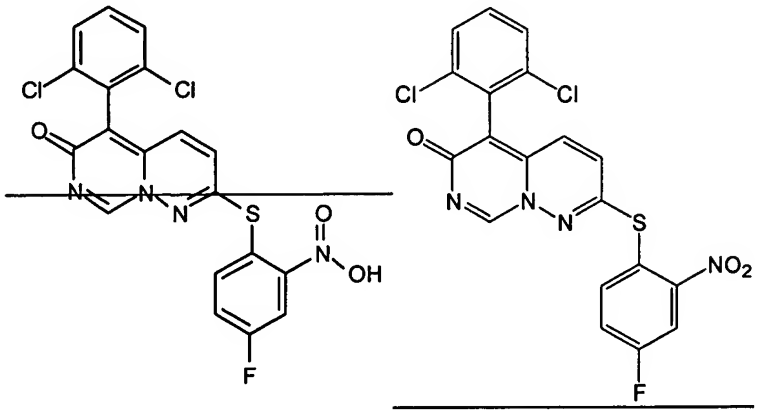




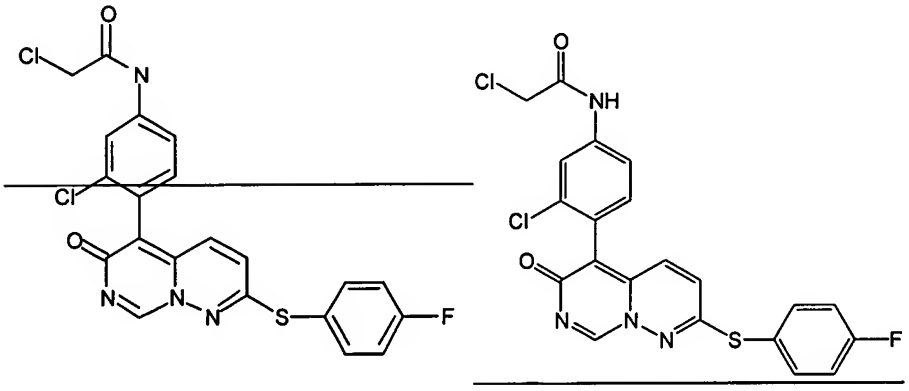
Please replace the paragraph beginning at page 11, line 11, with the following rewritten paragraph:

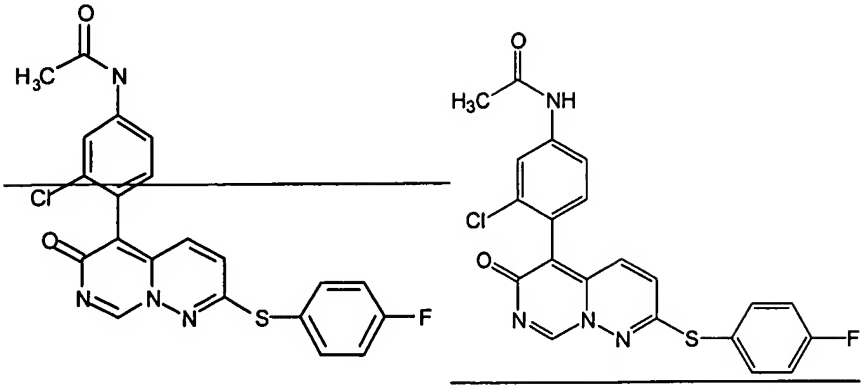
--According to a preferred embodiment, Q_2 is phenyl or pyridyl containing 0 to 3 substituents, wherein each substituent is independently selected from chloro, fluoro, bromo, methyl, ethyl, isopropyl, -OCH_3, -OH, -NH_2, -CF_3, -OCF_3, -SCH_3,[[-OCH_3,]] -C(O)OH, -$C(O)OCH_3$, -CH_2NH_2, -$N(CH_3)_2$, -CH_2-pyrrolidine and -CH_2OH.--

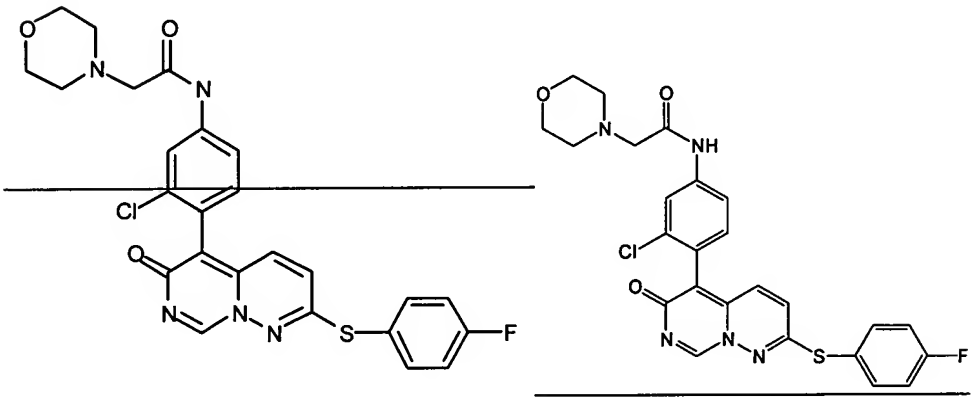
Please replace the chemical structure of compound 34, depicted at page 19, with the following redrawn chemical structure:



Please replace the chemical structures of compounds 49, 51, and 52, depicted at page 21, with the following redrawn chemical structures:







Please replace the paragraph beginning at page 22, line 19, with the following rewritten paragraph:

--Leaving group reagents of formula IIa that are useful in producing the p38 inhibitors of this invention include dimethylformamide dimethylacetal, dimethylacetamide dimethylacetal, trimethyl orthoformate, dimethylformamide diethylacetal and other related reagents. Preferably the leaving group ~~reagents~~ reagent of formula IIa used to produce the inhibitors of this invention is dimethylformamide dimethylacetal.--

Please replace the chemical structures of Table 2, depicted at pages 30-34, with the following redrawn chemical structures:

--Table 2. Formula Ic Compounds.

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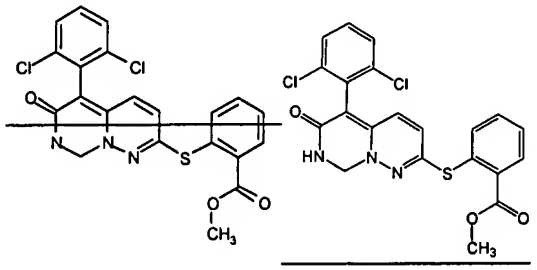
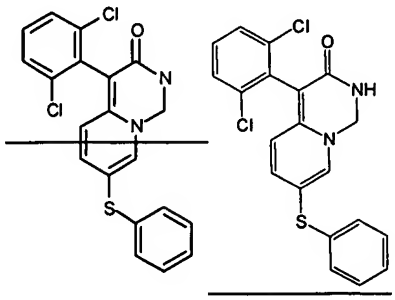
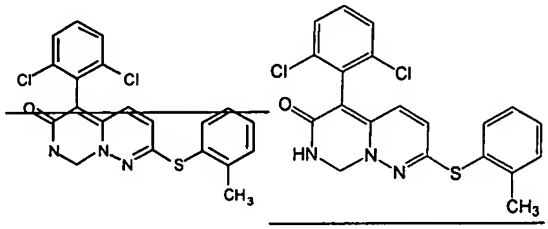
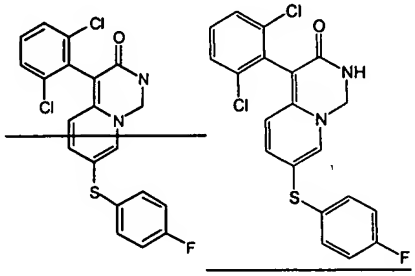
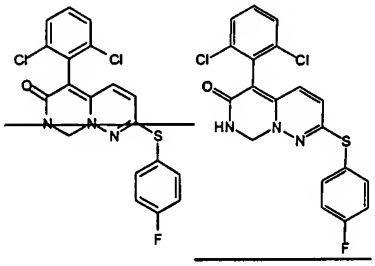
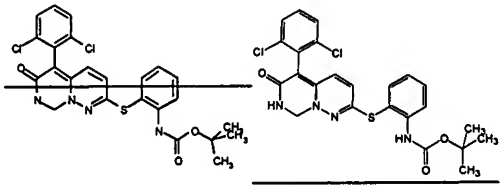
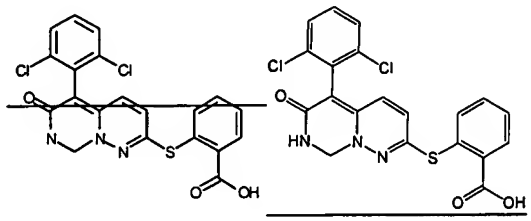
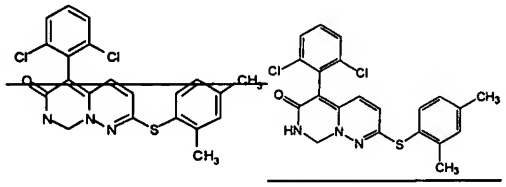
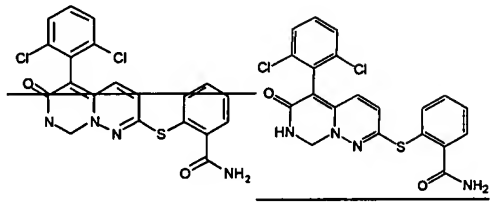
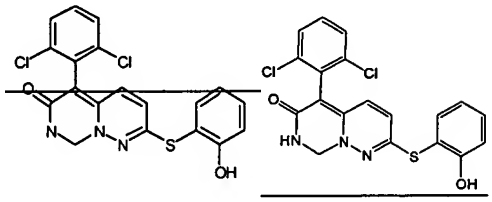
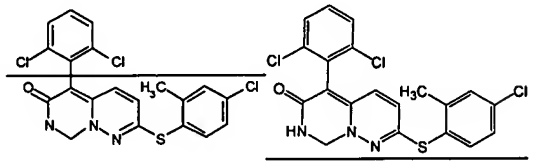
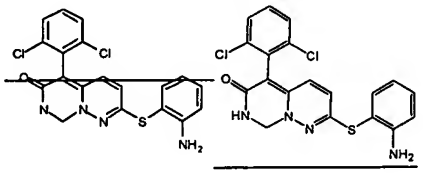
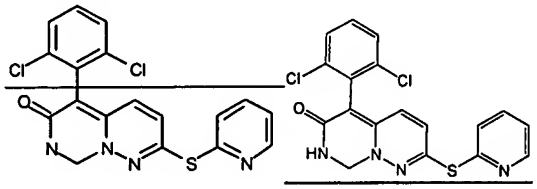
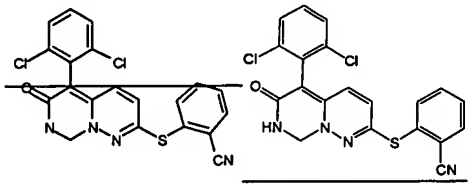
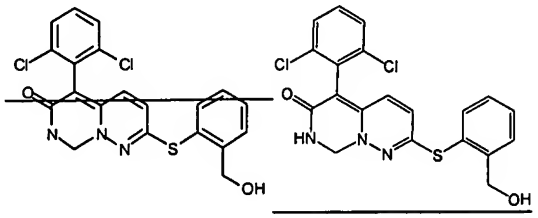
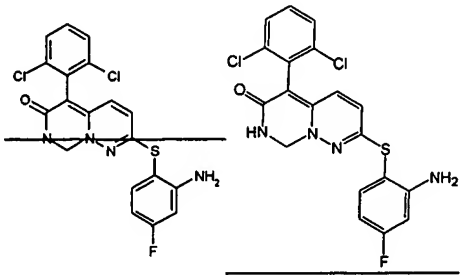
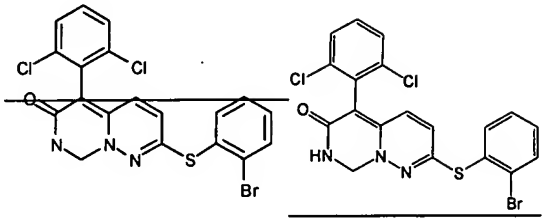
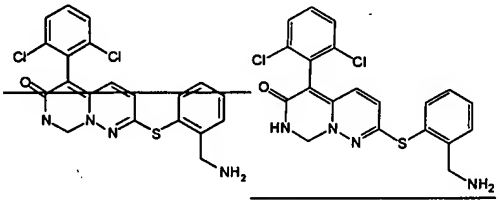
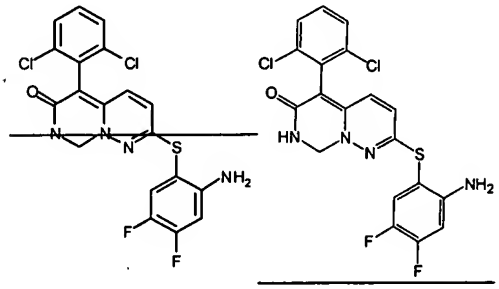
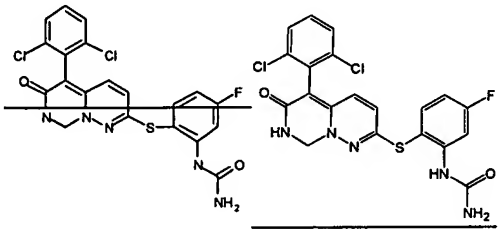
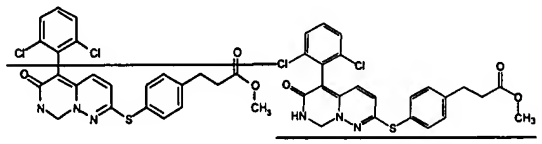
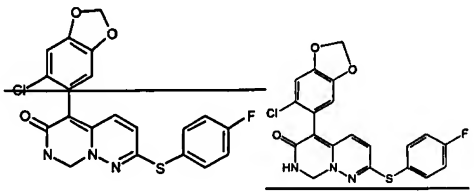
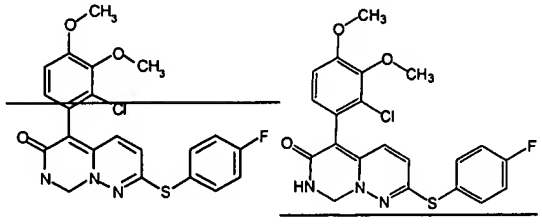
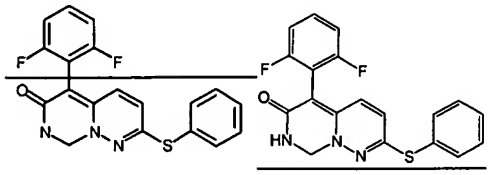
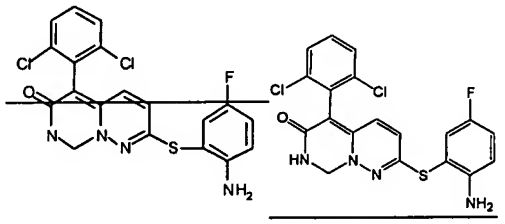
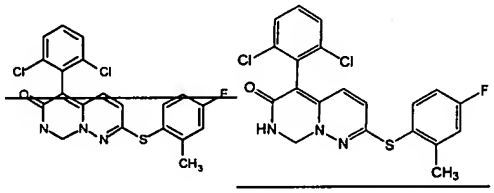
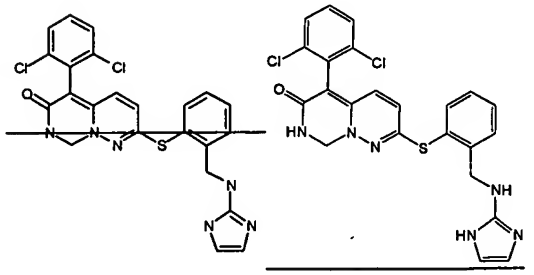
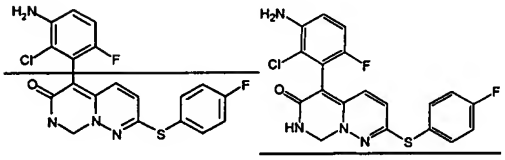
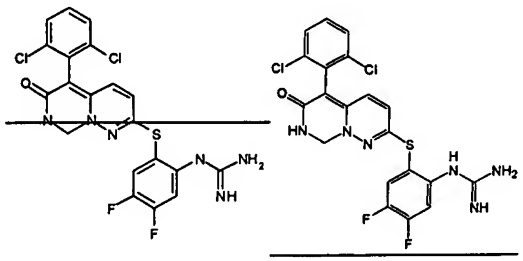
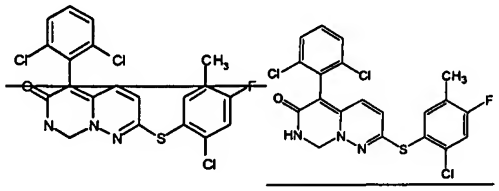
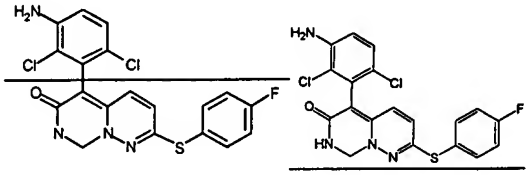
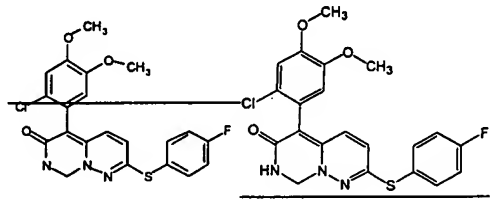
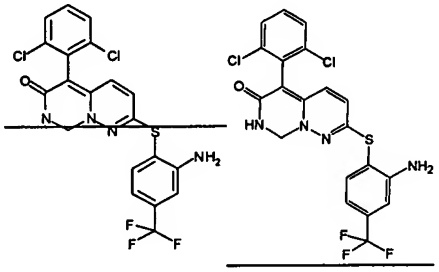
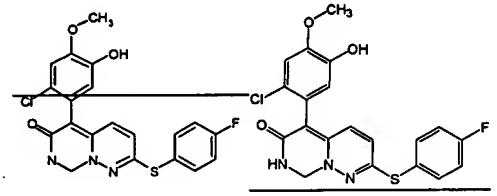
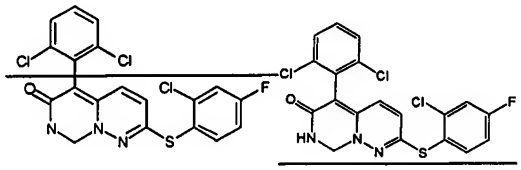
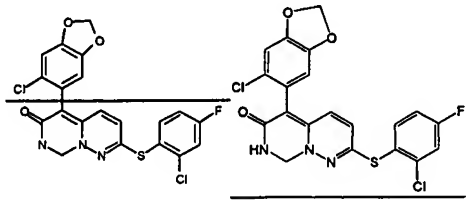
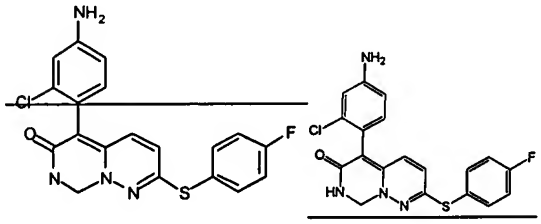
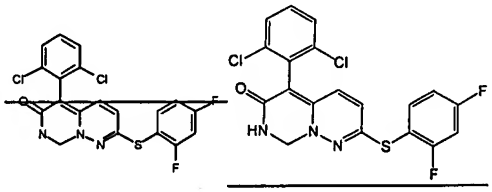
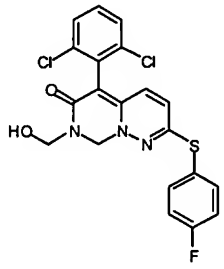
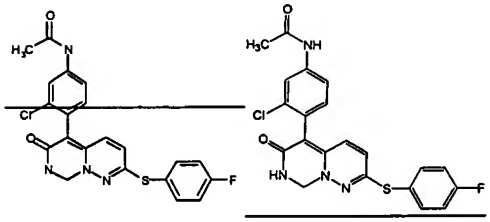
101		110	
102		111	
103		112	

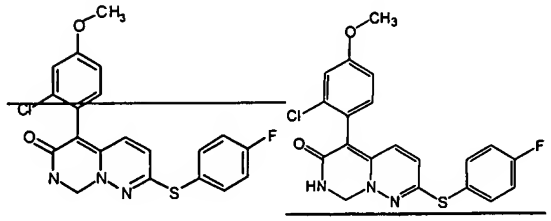
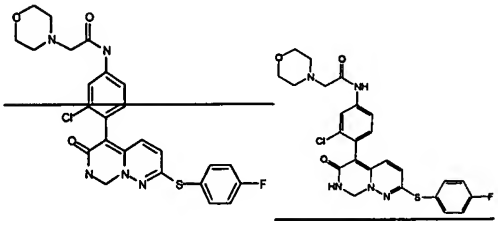
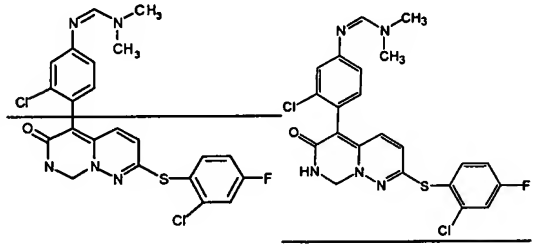
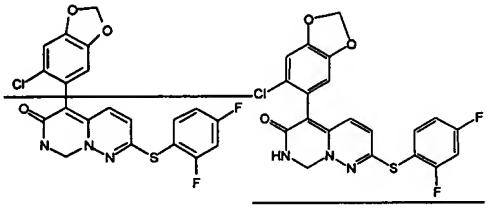
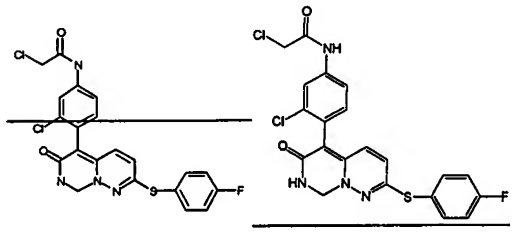
104		113	
cpd #	structure	cpd #	structure
105		114	
106		115	
107		116	

cpd #	structure	cpd #	structure
108		117	
109		118	
119		128	

120		129	
121		130	
122		131	
123		132	

124		133	
cpd #	structure	cpd #	structure
125		134	
126		135	

127		136	
137		142	
cpd #	structure	cpd #	structure
138		143	

139		144	
140		145	
141			

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Please replace the paragraph beginning at page 35, line 12, with the following rewritten paragraph:

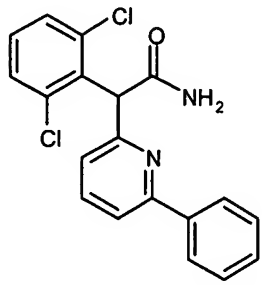
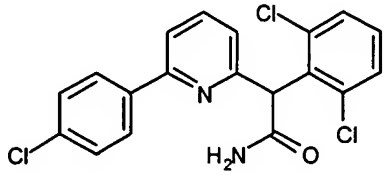
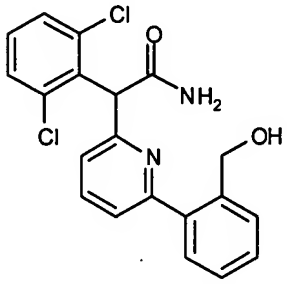
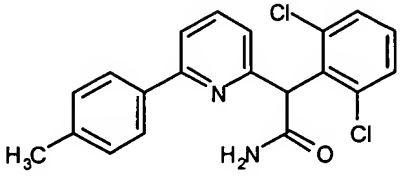
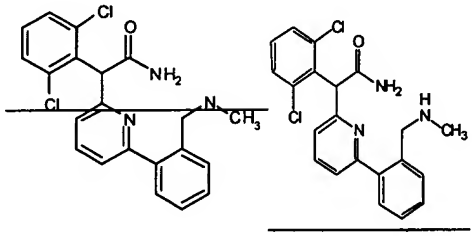
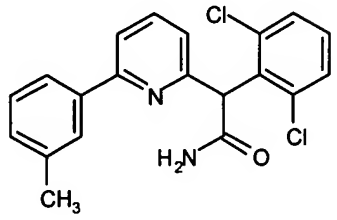
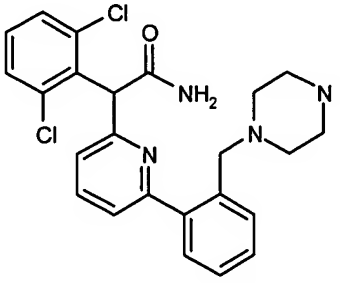
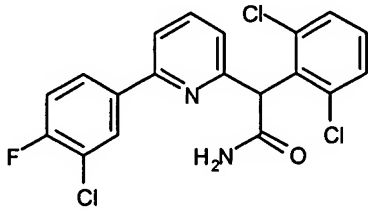
--Q_3 is a 5-6 membered aromatic carbocyclic or heterocyclic ring system, or an 8-10 membered bicyclic ring system comprising aromatic carbocyclic rings, aromatic heterocyclic rings or a combination of an aromatic carbocyclic ring and an aromatic heterocyclic ring. The rings of Q_3 are substituted with 1 to 4 substituents, each of which is independently selected from halo; C_1-C_3 alkyl optionally substituted with NR'_2, OR', CO_2R' or $CONR'_2$; O-(C_1-C_3)-alkyl optionally substituted with NR'_2, OR', CO_2R' or $CONR'_2$; NR'_2; OCF_3; CF_3; NO_2; CO_2R'; [[CONR']]CONHR'; SR'; $S(O_2)N(R')_2$; SCF_3; CN; $N(R')C(O)R^4$; $N(R')C(O)OR^4$; $N(R')C(O)C(O)R^4$; $N(R')S(O_2)R^4$; $N(R')R^4$; $N(R^4)_2$; OR^4; $OC(O)R^4$; $OP(O)_3H_2$; or [[N=C-$N(R')_2$]]N=CH-$N(R')_2$. --

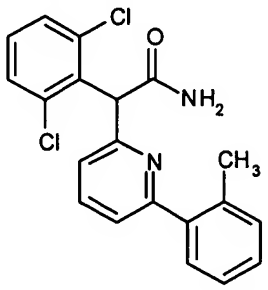
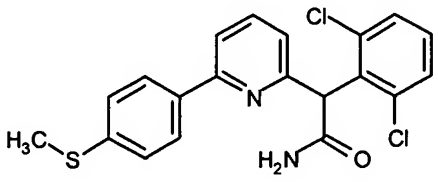
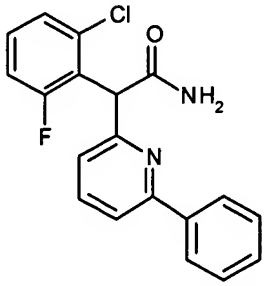
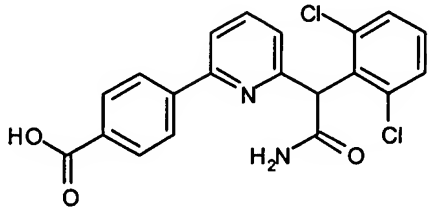
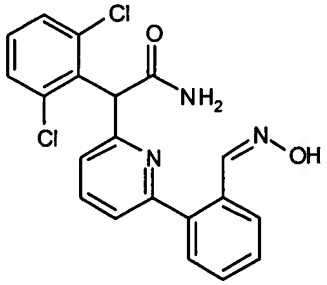
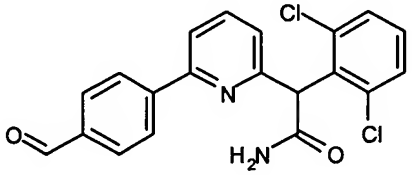
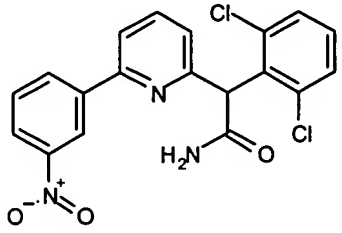
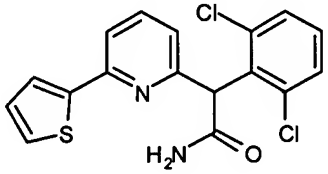
Please replace the paragraph beginning at page 36, line 12, with the following rewritten paragraph:

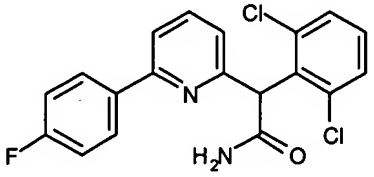
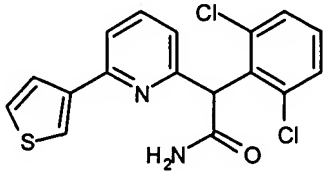
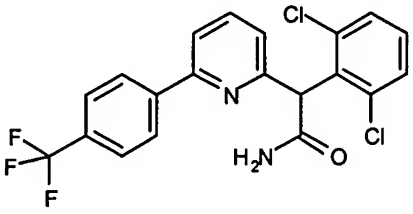
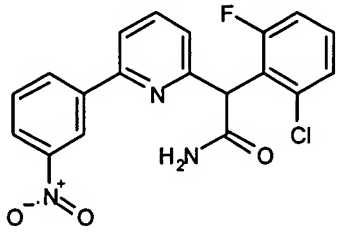
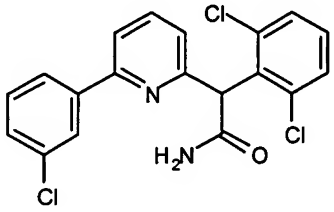
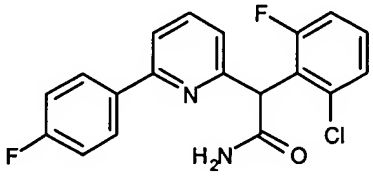
--According to another preferred embodiment, Q_3 is a monocyclic carbocyclic ring, wherein each ortho substituent is independently selected from halo or methyl. According to another preferred embodiment, Q_3 contains 1 or 2 additional substituents independently selected from NR'_2, OR', CO_2R' CN, $N(R')C(O)R^4$; $N(R')C(O)OR^4$; $N(R')C(O)C(O)R^4$; $N(R')S(O_2)R^4$; $N(R')R^4$; $N(R^4)_2$; OR^4; $OC(O)R^4$; $OP(O)_3H_2$; or [[N=C-$N(R')_2$]]N=CH-$N(R')_2$.--

Please replace the chemical structures of Table 4, depicted at pages 41-47, with the following redrawn chemical structures:

--Table 4. Formula Ig Inhibitors.

cpd #	structure	cpd #	structure
202/ 301		310	
302		311	
303		312	
304		313	

305		314	
cpd #	structure	cpd #	structure
306		315	
307		316	
308		317	

309		318	
319		328	
320		329	
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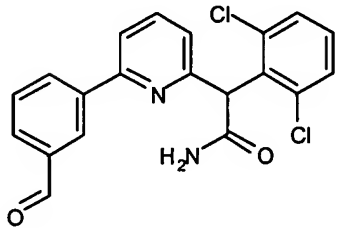
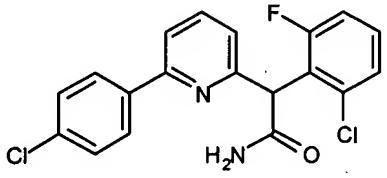
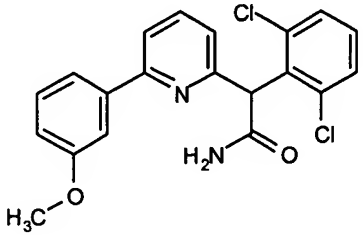
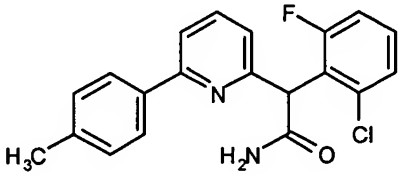
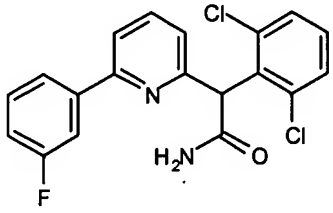
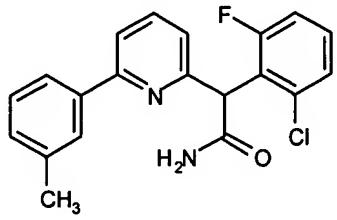
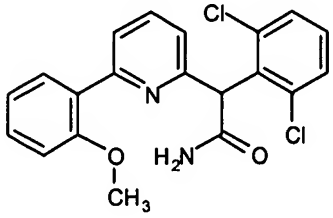
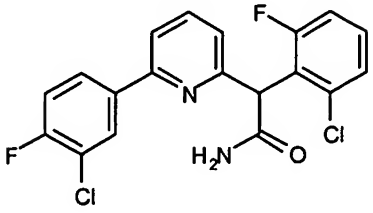
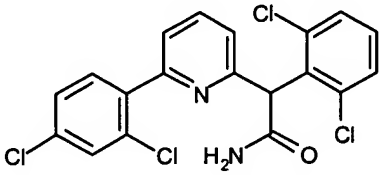
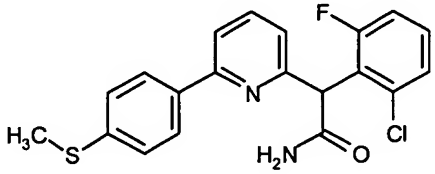
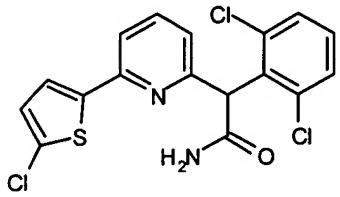
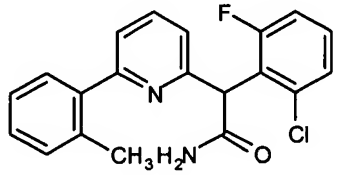
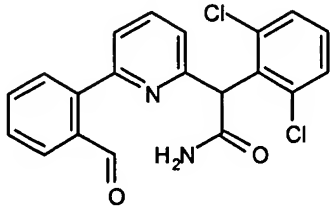
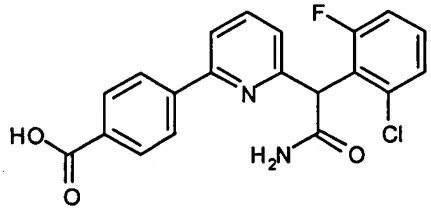
321		330	
322		331	

323		332	
324		333	
325		334	
326		335	
327		336	
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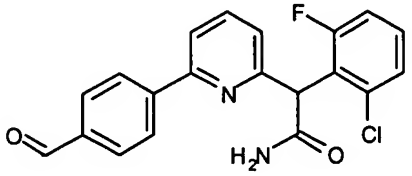
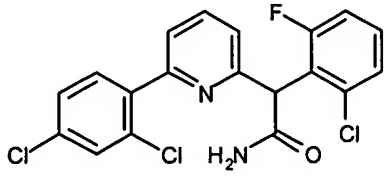
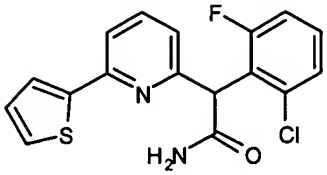
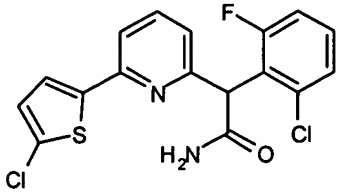
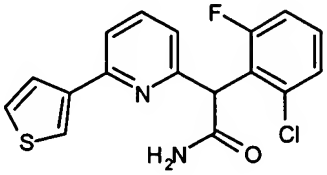
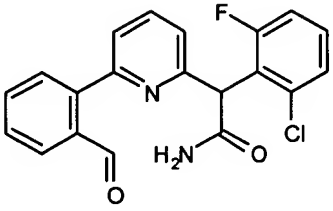
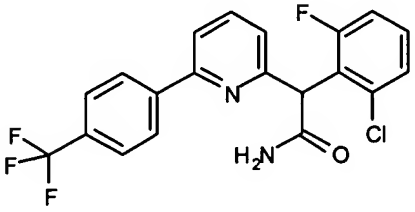
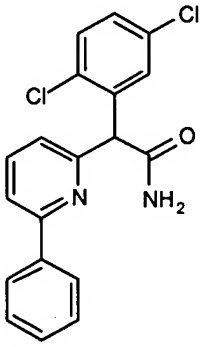
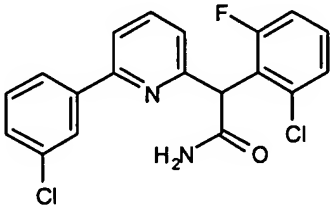
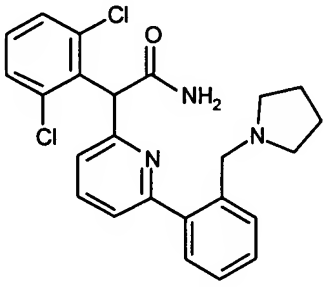
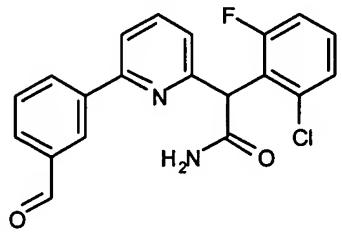
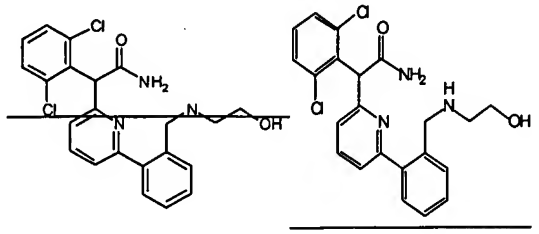
337		346	
338		347	
339		348	
340		349	
341		350	

342		351	
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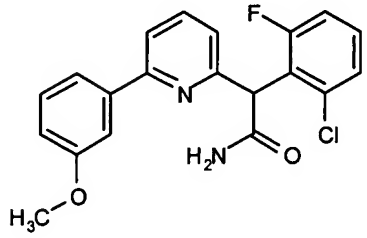
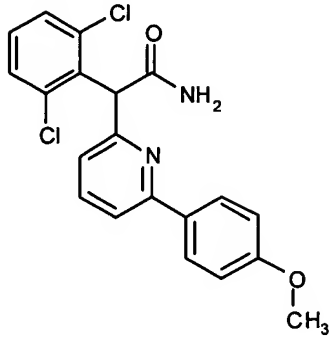
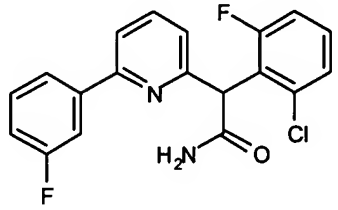
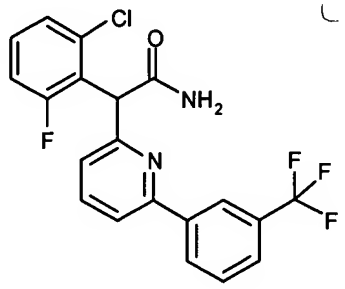
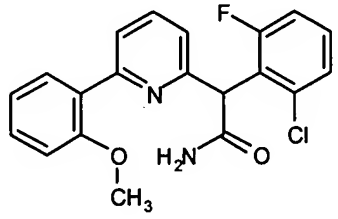
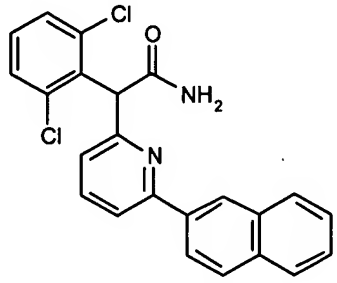
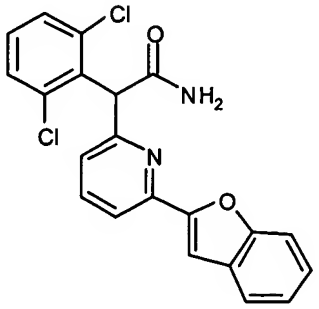
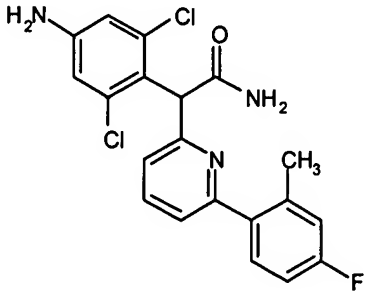
343		352	
344		353	
345		354	

355		364	
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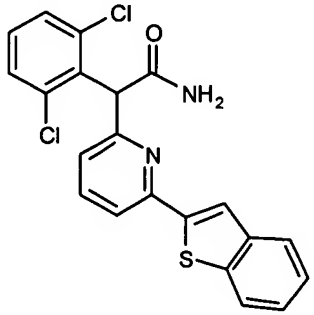
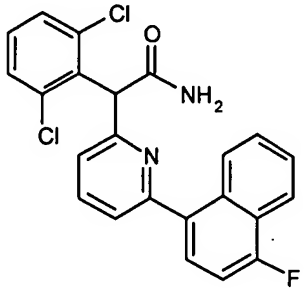
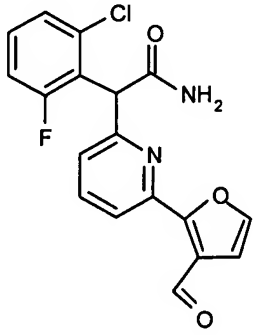
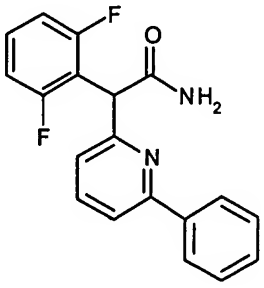
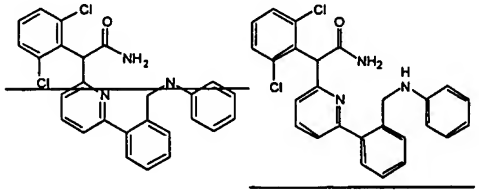
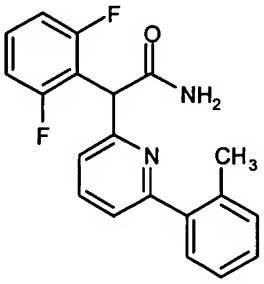
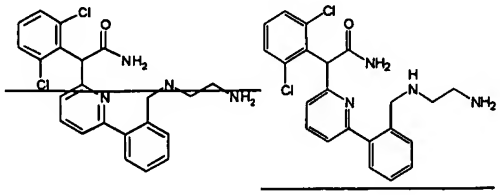
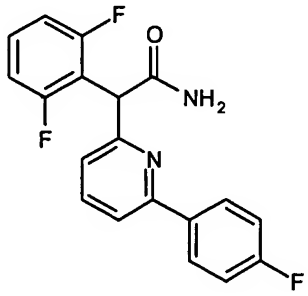
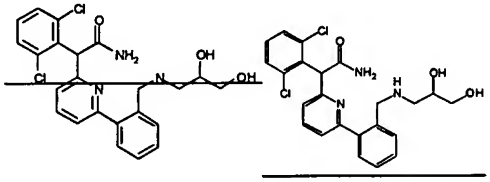
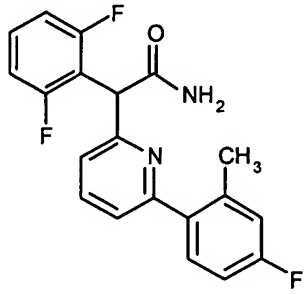
356		365	
357		366	
358		367	

359		368	
360		369	
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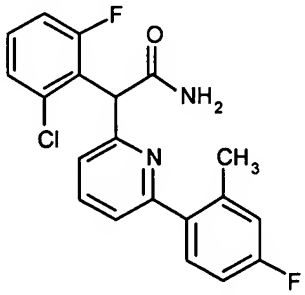
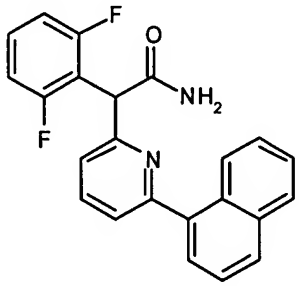
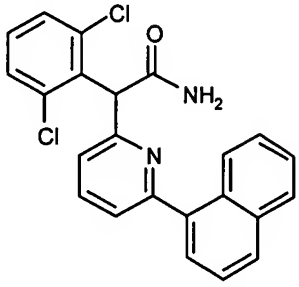
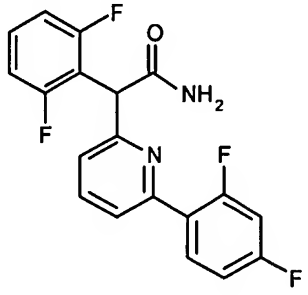
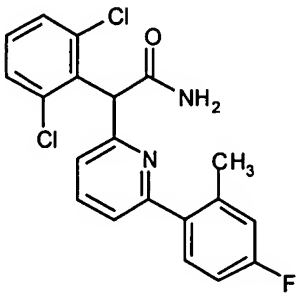
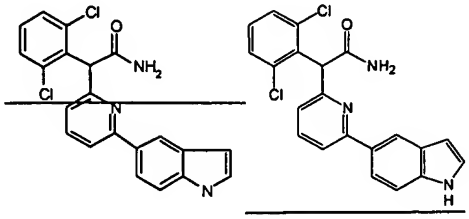
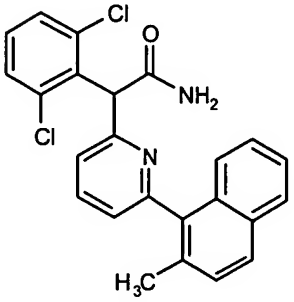
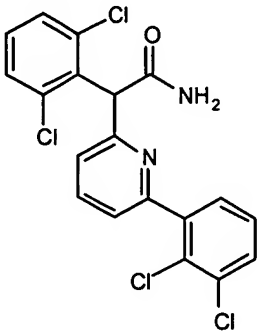
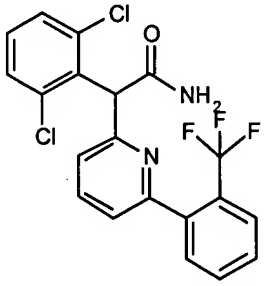
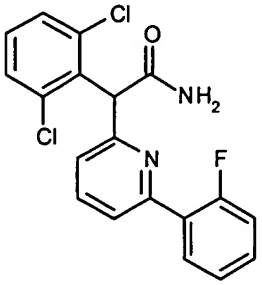
361		370	
362		371	

363		372	
373		382	
374		383	
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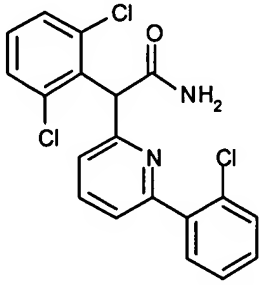
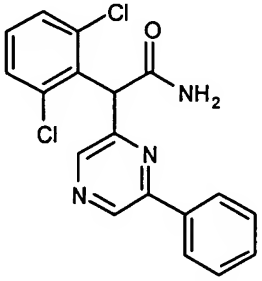
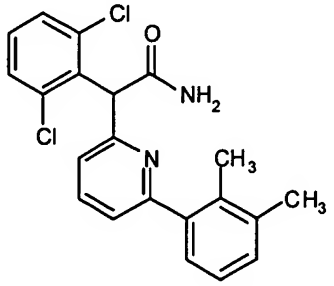
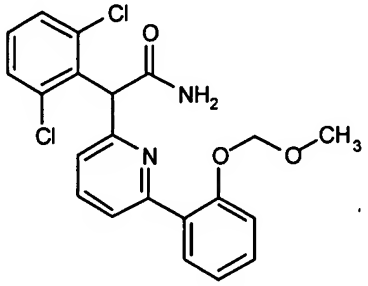
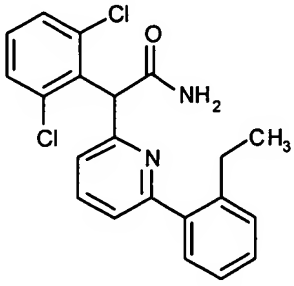
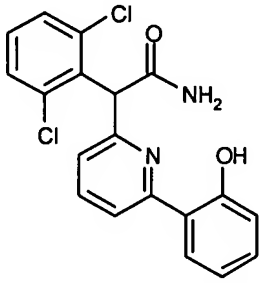
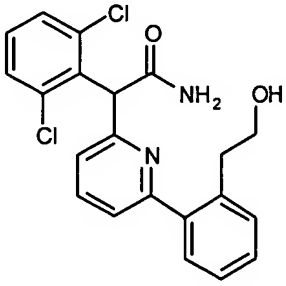
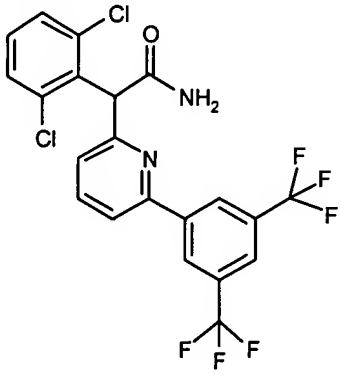
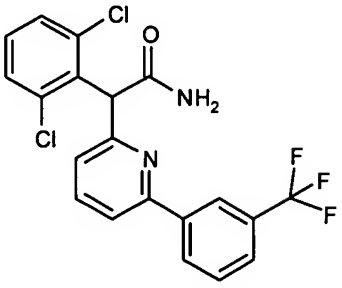
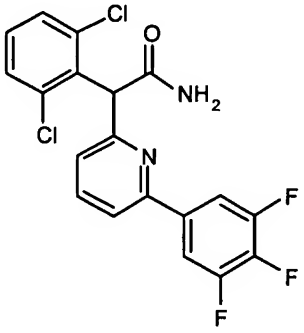
375		384	

376		385	
377		386	
378		387	
379		388	
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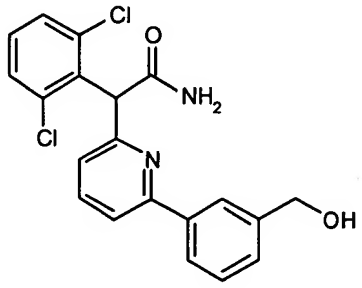
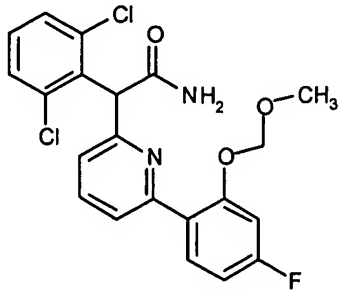
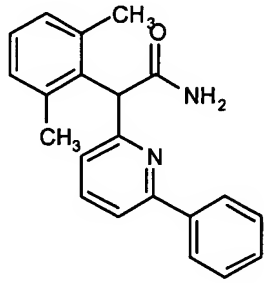
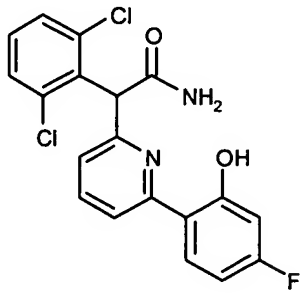
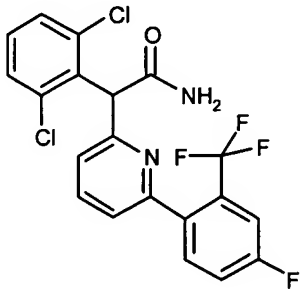
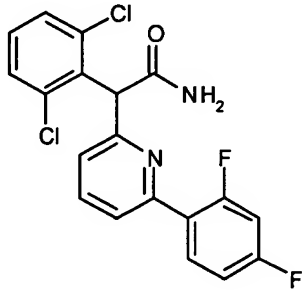
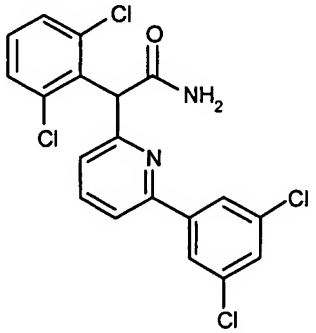
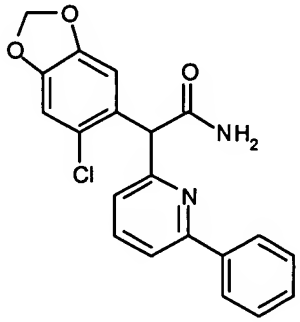
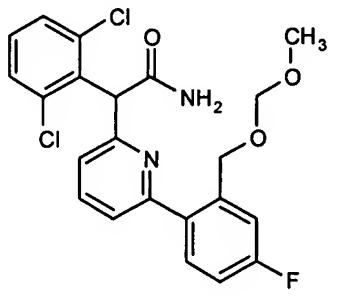
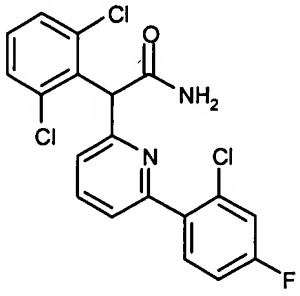
380		389	
381		390	
391		396	
392		397	

393		398	
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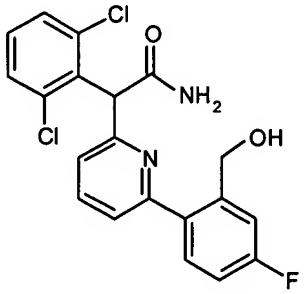
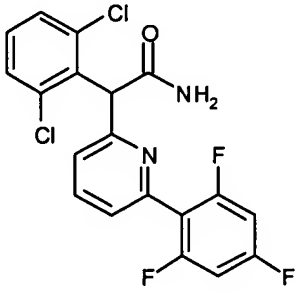
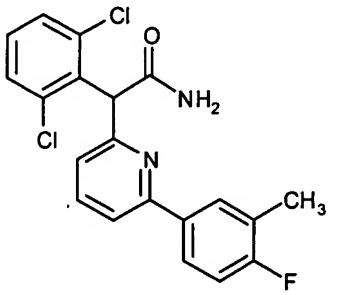
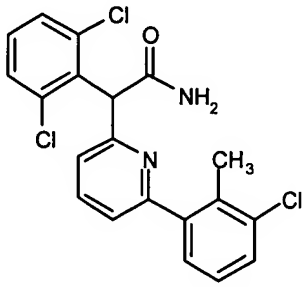
394		399	
395		1301	

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Please replace the paragraph beginning at page 52, line 20, with the following rewritten paragraph:

--An *in vivo* assay useful for determining the inhibitory activity of the p38 inhibitors of this invention[[are]] is the suppression of hind paw edema in rats with *Mycobacterium butyricum*-induced adjuvant arthritis. This is described in J.C. Boehm et al., J. Med. Chem., 39, pp. 3929-37 (1996), the disclosure of which is herein incorporated by

reference. The p38 inhibitors of this invention may also be assayed in animal models of arthritis, bone resorption, endotoxin shock and immune function, as described in A. M. Badger et al., J. Pharmacol. Experimental Therapeutics, 279, pp. 1453-61 (1996), the disclosure of which is herein incorporated by reference.--

Please replace the paragraph beginning at page 53, line 8, with the following rewritten paragraph:

--The term "p38-mediated condition", as used herein means any disease or other deleterious condition in which p38 is known to play a role. This includes, conditions which are known to be caused by IL-1, TNF, IL-6 or IL-8 overproduction. Such conditions include, without limitation, inflammatory diseases, autoimmune diseases, destructive bone disorders, proliferative disorders, infectious diseases, neurodegenerative diseases, allergies, reperfusion/ischemia in stroke, heart attacks, angiogenic disorders, organ hypoxia, vascular hyperplasia, cardiac hypertrophy, thrombin-induced platelet aggregation, and conditions associated with prostaglandin ~~endoperoxidase~~ endoperoxide synthase-2.--

Please replace the paragraph beginning at page 57, line 14, with the following rewritten paragraph:

--Salts derived from appropriate bases include alkali metal (e.g., sodium and potassium), alkaline earth metal (e.g., magnesium), ammonium and N-~~(C1-4 alkyl)4+~~(C_{1-4} alkyl)$^{4+}$ salts. This invention also envisions the quaternization of any basic nitrogen-containing groups of the compounds disclosed herein. Water or oil-soluble or dispersible products may be obtained by such quaternization.--

Please replace the paragraph beginning at page 65, line 12, with the following rewritten paragraph:

--A solution of pre-1 from step C. (0.22 g., 0.69 mmol) and N,N-dimethylformamide dimethylacetal (0.18 g., 1.5 mmol) in toluene (5 ml) was heated at 100° C for one hour. Upon cooling, the resulting solid was filtered and dissolved in warm ethyl acetate. The product was precipitated with the dropwise addition of diethyl ether. The product was then filtered and washed with diethyl ether to give 0.038 g. of compound 1 ~~(which is depicted in Table 1)~~ as a yellow solid. ^{1}H NMR (500 MHz, CDCl3) d8.63 (s), 7.63 - 7.21 (m), 6.44 (d).--

Please replace the paragraph beginning at page 81, line 3, with the following rewritten paragraph:

--In a flame-dried 100 ml round-bottomed flask, 2.28 g (93.8 mmol) of magnesium chips were added to 50 ml of anhydrous tetrahydrofuran. One crystal of iodine was added forming a light brown color. To the solution was added 1.5 ml of a 10.0 ml (79.1 mmol) sample of 2-bromo-5-fluorotoluene. The solution was heated to reflux. The brown color faded and reflux was maintained when the external heat source was removed indicating Grignard formation. As the reflux subsided, another 1.0 - 1.5 ml portion of the bromide was added resulting in a vigorous reflux. The process was repeated until all of the bromide had been added. The olive-green solution was externally heated to reflux for one hour to ensure complete reaction. The solution was cooled in an ice-bath and added via syringe to a solution of 9.3 ml (81.9 mmol) of trimethyl borate in 100 ml of tetrahydrofuran at -78°C. After the

Grignard reagent had been added, the flask was removed from the cooling bath and the solution was stirred at room temperature overnight. The grayish-white slurry was poured into 300 ml of H_2O and the volatiles were evaporated in vacuo. HCl (400 ml of 2N solution) was added and the milky-white mixture was stirred for one hour at room temperature. A white solid precipitated. The mixture was extracted with diethyl ether and the organic extract was dried ($MgSO_4$) and evaporated in vacuo to afford 11.44 g (94%) of the boronic acid as a white solid.-

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Please replace the paragraph beginning at page 86, line 18, with the following rewritten paragraph:

--dimethylaminoacet[[a]]yl prodrug of compound 103--

Please replace the paragraph beginning at page 106, line 2, with the following rewritten paragraph:

--For kinase IC50 values, "+++" represents [[>]]$\leq$0.1 μM, "++" represents between 0.1 and 1.0 μM, and "+" represents [[<]]$\geq$1.0 μM. For cellular IL-1 and TNF values, "+++" represents [[>]]$\leq$0.1 μM, "++" represents between 0.1 and 0.5 μM, and "+" represents [[<]]$\geq$0.5 μM. For all whole blood ("WB") assay values, "+++" represents [[>]]$\leq$0.25 μM, "++" represents between 0.25 and 0.5 μM, and "+" represents [[<]]$\geq$0.5 μM. In all assays indicated in the table above, "N.D." represents value not determined.--